of quadratojugals, dermosupraoccipitals and tabulars has been definitely determined, and the supratemporals almost as definitely, thus giving to the genus nearly every skull element found in the most primitive cotylosaurs. The mandibles may be a little less slender and there may be fewer teeth but one can say with assurance that were an isolated skull of *Sphenacodon* found in Texas it would be referred unhesitatingly to *Dimetrodon.* And this similarity extends to other parts of the skeleton, with the exception of the spines of the vertebrae.

Many and various have been the conjectures offered to explain the extraordinary spines in *Dimetrodon.* In my opinion nothing better has been suggested than that of Professor Case, namely, that they represent an ornamental or senile character of the race, of no profound importance in the life economy of the animals. Certainly, as I have previously observed, if the spines of *Dimetrodon* had been of important use to their possessors they must have produced correlated differences in other parts of the skeleton. The differences in the spines have no more than a generic value.

There are doubtless several species of *Sphenacodon* in the New Mexican beds, but the known remains from the Baldwin and Miller bonebeds seem all to belong to one species. From different horizons on the Puerco, however, large specimens are known, now preserved in the Yale Museum. The present specimen, which doubtless belongs to *S. ferox* Marsh, was nearly five feet long as figured. The Yale specimens indicate a form one-half larger, or about seven and a half feet in length, or of about the size of most specimens referred to *Dimetrodon incisivus.* *Sphenacodon* is definitely known only from the valley of the Puerco and its tributaries in New Mexico; not a fragment of it has been found in the El Cobre deposits scarcely a score of miles away. However, there are specimens in the Chicago collection from Texas that suggest very strongly its occurrence there, but definite proof is lacking.

ON VOLUME IN BIOLOGY

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In one respect this subject is time-honored. Herbert Spencer and many others since his day have recognized the biological importance of the principle of similitude. Bulk increases as the cube of length; surface as the square. Hence the limitation of the size of cells, the

minute canalization of the body, and the prodigious jumps of the flea, as well as the variation in metabolism with the size of the organism. Yet even this subject is by no means exhausted. For example (a fact which appears to be of some importance in describing the internal regulation of temperature) the difference in temperature between center and surface of a sphere which is producing heat uniformly throughout its whole mass, when equilibrium has been established with a surrounding liquid medium of constant temperature, is proportional to the square of the radius.[1]

But apart from this great principle and certain superficial discussions of the nature of oedema and similar phenomena, the regulation of volume has remained without any physico-chemical analysis. Yet, from the standpoint of physical science, this is perhaps the most universal and fundamental of all organic regulations. I believe that this strange neglect may be traced to three facts. In the first place, the chemist is accustomed to vary the volume of his systems to suit his convenience. This is a justifiable practice, because, if the phases are so large that capillary phenomena may be disregarded, and so small that gravity need not be taken into account, the division of a phase into two parts does not change its energy. Thus, volume hardly enters into our calculations except as an indirect expression for that which is regarded as the true variable, viz., concentration. This, however, is to disregard the real question as it presents itself in biology. Secondly, *when equilibrium has been established* in a heterogeneous system, as Willard Gibbs rigorously proved, the volume of the phases—capillary and gravitational phenomena being absent—is not relevant to the state of the system. But it may be at once observed, first, that until equilibrium has been attained the volume is of great moment, and, secondly, that equilibrium is never attained within the organism. Finally, the ordinary conception of the process of diffusion is based upon a mathematical discussion, which, though leading to a consistent description of the phenomena, is nevertheless a false representation of the actual occurrences. And nearly all physiological changes of volume depend upon diffusion.

Contrary to a general though vague belief, the regulation of volume is theoretically independent of osmotic pressure regulation. For example, if a kidney produces a liter of urine of the same freezing point as blood, it must have diminished the volume of the body and left the osmotic pressure sensibly unchanged.

For the purpose of discussion, the activity of the kidney may be reduced to the following fiction: First there must be an excretion of all

the dissolved constituents of blood plasma, including water itself, in such amounts as to bring the composition of the blood in all respects to a hypothetical normal composition; secondly, a certain portion of this normal plasma, minus the colloids, must be removed in order to regulate the volume.

Statistically the volume of the urine must vary with the magnitude of the volume regulation, although, in particular cases, it need bear no relation to this quantity. Now sodium chloride is the principal constituent of blood plasma. Hence, statistically the ratio $\Delta : NaCl$ (i.e. the ratio of freezing point depression to sodium chloride concentration in urine) will be small when the volume is large, and large when the volume is small. Thus we arrive at a theoretical deduction *a priori* of Korányi's coefficient.[2] This coefficient tells us, therefore, nothing about the mode of action of the kidney mechanism. It has no bearing on the question of the functions of glomeruli and tubules. For the ratio is seen to be, as existing evidence proves, necessarily liable to indefinite fluctuations in particular cases. There is involved merely a statistical truth, expressing the conditions under which any kidney must operate in case sodium chloride is the chief constituent of the blood.

The practical importance of this theoretical discrimination of volume regulation from the excretion of the several urinary constituents appears to be established by the fact that in pathological conditions the daily volume of urine may be constant during variations in amounts of water or salt ingested, even when such experiments lead to fluctuations in the physico-chemical properties of the urine.[3] For this shows that the regulation of volume may be deranged more or less independently of the proper excretory functions.

If the final stage of volume regulation has been neglected, the intermediate stages have been generally misconceived. Neither the swelling of colloids nor the pressure which results from osmosis can furnish the basis for an analysis of such phenomena. In their stead we must turn to the kinetic theory and to Willard Gibbs' thermodynamics. But it should be first remarked that osmotic 'pressure' and colloidal swelling 'pressure' hardly act as important sources of mechanical tension, in the living organism. Even oedema involves very small magnitudes of such pressures. Secondly, changes in volume merely consist in the passage of material from one phase to another (except in so far as physical and chemical changes within a phase may produce very slight fluctuations in volume). Finally, apart from the operation of special secretory mechanisms which we do not understand, such processes

consist in the diffusion through phases and across interfaces from points of higher to points of lower potential. In the internal phenomena no less than in the exchanges with the environment, and in the internal phenomena of a single phase no less than in the heterogeneous process, water is quite as much in question as the dissolved substances.

This fact has been generally overlooked, by the physicists even more than by the physiologists. We may consider a simple diffusion experiment in which a layer of water is placed above a layer of sugar solution. It is true that the sugar must diffuse up into the water, but it is also true that the water must diffuse down into the solution. Yet the phenomena of diffusion have always been discussed with the help of the mathematical theory of heat conduction as exactly defined by Fourier. Thus Fick's theory of diffusion overlooks the rôle of the solvent. This has been possible because the process takes place *as if* the solvent were inert and the dissolved substance possessed a higher diffusibility. But the diffusion of the solvent is probably greater than that of the solute, in that water is, with a few exceptions, the most diffusible of substances. In their neglect of the relativity of motion, contemporary accounts of diffusion involve an old fallacy that occurs even in the astronomy of Ptolemy.

It may perhaps be objected that throughout the organism water exists at a uniform potential. This, however, is both untrue and beside the point. For, if two phases are free to exchange material, an exchange involving all their components will take place unless, at the outset, all their components possess the same potential in both phases. Thus, as Höber[4] has shown, isotonic solutions of sodium chloride and magnesium sulphate change in volume when brought into contact. For the chloride diffuses faster than the sulphate. Thus the sulphate solution becomes more concentrated and, as a result, water diffuses into it from the chloride solution. In like manner differences of pressure and of temperature influence the potential of water and of all dissolved substances. Finally, the processes of metabolism are continually altering the concentrations of solutions, and therefore the potential of water.

When these facts are taken into account, it becomes clear that the chief physical factor in the internal regulation of volume is water, through its distribution between the infinite assemblage of phases which make up the organism. The general concepts of the phase rule reveal the several elements of this process—except those which depend upon so-called selective activities—but the physical theory of diffusion, and therefore the whole kinetic description, has been developed from a

false representation of the process, which neglects the movements of water itself. Only when this is immediately evident, as in osmotic phenomena, is it at all taken into account. But even here the current explanations are often incomplete. And the general theory of the diffusion of water is almost useless for the purposes of physiology. Yet there seems to be no reason to doubt that, in the organism, this is the most important process of diffusion.

[1] I am indebted to Prof. W. E. Byerly for kindly calculating the value of this difference which is $p/k \cdot r^2/6$, where p is rate of heat production, k conductivity, and r the radius.

[2] A. v. Korányi, *Zs. Klin. Medizin*, 33, 1892, and Korányi und Richter, *Physikalische Chemie und Medizin*, Leipzig, 1908, 2, pp. 133–224.

[3] *Ibid.*, pp. 165, 166.

[4] *Pflüger's Archiv*, 74, 225 (1899).